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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,903	07/10/2001	Avi Ashkenazi	10466/69	1524

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EXAMINER

BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/902,903

Applicant(s)

ASHKENAZI ET AL.

Examiner

Bridget E. Bunner

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-- **Th MAILING DATE** f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>12, 13</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 04 March 2003 (Paper No. 17) has been entered in full. Claims 39 is amended and claim 44 is cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 39-43 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the declaration at pg 2 of the previous Office Action (Paper No. 11, 03 October 2002) is *withdrawn* in view of the submitted Application Data Sheets (27 December 2002; 04 March 2003).
2. The objections to the specification at pg 2 of the previous Office Action (Paper No. 11, 03 October 2002) is *withdrawn* in view of the amended specification (Paper No. 17, 04 March 2003).
3. The rejection to claims 39-44 under 35 U.S.C. 112, second paragraph, as set forth at pg 6-7 of the previous Office Action (Paper No. 11, 03 October 2002) is *withdrawn* in view of amended claim 39 (Paper No. 17, 04 March 2003).

Claim Rejections - 35 USC § 101 and 35 USC § 112

4. Claims 39-43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive

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experimentation. The basis for this rejection is set forth for claims 39-44 at pg 3-6 of the previous Office Action (Paper No. 11, 03 October 2002).

5. Claims 39-43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth for claims 39-44 at pg 5-6 of the previous Office Action (Paper No. 11, 03 October 2002).

Specifically, claims 39-43 are directed to an antibody that specifically binds to the polypeptide shown in Figure 86 (SEQ ID NO: 245). The claims also recite that the antibody is monoclonal or humanized. The claims recite that the antibody is an antibody fragment or that the antibody is labeled.

Applicant's arguments (Paper No. 17, 04 March 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the antibodies claimed in the present application have a specific, substantial, and credible asserted utility, which is sufficiently described in the specification. Applicant indicates that the PDB12 cell inhibition data at pg 207 of the specification is relied on in support of patentable utility. Applicant contends that Example 70 of the specification describes a cell based assay in which PRO293 polypeptide inhibits protein production by PDB12 pancreatic ductal cells using an AlamarBlue™-based cell proliferation assay. Applicant indicates that the assay described in Example 70 uses fluorescence read-out, which allows one to calculate total cellular protein concentration produced by PDB12 pancreatic ductal cells in the presence and absence of a particular test molecule, such as the PRO293 polypeptide. Applicant

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argues that agonist antibodies specifically binding the PRO293 polypeptides are useful drug candidates in the treatment of pancreatic disorders, where such inhibition is desirable, such as pancreatitis, e.g. chronic alcoholic pancreatitis, which is known to be accompanied by ethanol-induced protein secretory alteration, and increased intraductal protein precipitation. Applicant also asserts that antagonist anti-PRO293 antibodies find utility, for example, in the diagnosis of such diseases. It is noted that Applicant cites the Utility Examination Guidelines, 66 Fed. Red. 1092 (2001).

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, as discussed in the previous Office Action, Example 70 at pg 207 of the instant specification does not teach any specific resulting cell numbers or percentages, statistical differences, or the number of repetitions for the assay. The specification also does not disclose the quantity of PRO293 that is utilized in the assay. It is recognized in the art that cell growth/inhibition assays usually implement a variety of concentrations of the compound or protein of interest. Therefore, due to little or no guidance in the specification, the skilled artisan could conclude that PRO293 was utilized at toxic levels in the assay, which killed the PDB12 pancreatic ductal cells rather than showing an inhibition in protein production. Additionally, the specification does not teach any methods or working examples that utilize a different cell type or different growth factors/inhibitors as controls. The assay in the specification also does not measure protein production every day the cells are in culture. The specification only teaches that that cells are incubated for 4 days and then Alamar Blue Dye is added to each well (pg 207, lines 9-10). According to the vague results listed in this example, one skilled in the art might predict that the pancreatic ductal cells simply started to naturally die off, with the PRO293 protein

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having no effect on cell inhibition/proliferation or inhibition of protein production. Furthermore, any slight decrease in protein production, which may even result from the normal variations in cell number, would not indicate that PRO293 specifically inhibits protein production. Without any specific knowledge, which could not be obtained from the instant specification, one of ordinary skill in the art at the time the invention was made would not have been able to use the information obtained from this assay in a useful manner. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, therefore both polypeptide and their antibodies have no patentable utility.

Although Applicant argues that agonist anti-PRO293 antibodies would be useful drug candidates in the treatment of pancreatic disorders wherein such inhibition is desirable, such an asserted utility is not specific or substantial. The specification does not disclose any disorders which involve protein secretion by the pancreas which are associated with an altered level or form of the PRO293 protein encoded by the claimed polynucleotides. However, in the absence of any disclosed relationship between the PRO293 polypeptides and any disease or disorder, any information obtained from an *in vitro* cell assay would only serve as the basis for further research on the observation itself. Additionally, if anti-PRO293 antibodies were to be utilized as drug candidates, significant further experimentation would be required of the skilled artisan to determine the optimal quantity, duration, and method of administration. The specification does not disclose any methods or working examples indicating that anti-PRO293 antibodies treat or ameliorate any medical condition in a subject. Thus, the instant application has failed to provide

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guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the antibodies that specifically bind PRO293 polypeptides.

With regard to treatment or diagnosis of disease, in order for antagonist anti-PRO293 antibodies to be useful, as asserted, for treatment or diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the PRO293 polypeptide and a disease or disorder. Since the instant specification does not disclose presence or association of the PRO293 with any specific cell or tissue, there is not sufficient for establishing a utility in the treatment or diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the PRO293 polypeptide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the PRO293 polypeptide is either present only in diseased tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed antibodies against the PRO293 polypeptide as diagnostics for diseases. However, in the absence of any disclosed relationship between the PRO293 polypeptides and any disease or disorder and the lack of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from a protein inhibition assay would only serve as the basis for further

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research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

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Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
May 6, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER